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AN OVERVIEW OF SALIVARY DUCT CARCINOMA WITH EMPHASIS ON DIAGNOSIS AND TREATMENT.

Oncopathology

Dr Anindita Mondal	Senior Resident: Dept. of Pathology: IPGME&R, SSKM Hospital
Dr. PiyaliKundu	Demonstrator: Dept. of Pathology: IPGME&R, SSKM Hospital
Dr Prabhat Mahato	Junior Resident:Dept. of Pathology: IPGME&R, SSKM Hospital
Dr. Madhumita Mondal*	Assistant Professor:Dept. of Pathology : IPGME&R, SSKM Hospital *Corresponding Author

ABSTRACT

The aims and objectives of our study is to enlighten and summarize the clinical, histopathological features and immunihistochemical features of Salivary duct carcinoma with emphasis on the prognostic and treatment modalities.Between 2017 and 2021, out of 142 cases of salivary gland neoplasms in our tertiary care hospital, 11 cases of salivary gland neoplasms histopathologically diagnosed with SDC, were identified .The present study both prospectively and retrospectively analysed the clinicopathological and immunohistochemical data of these 11 cases and we found that the parotid gland was most common site for SDC affecting mostly smokers and males. 7 out of 11 study subjects had nerve paralysis which is 63.6% of the cases reflecting the aggresiveness of this tumour. In the current series of patients, distant metastasis occurred in 3 patients, with the lung found as the metastatic site. In our study, the protein expression levels of HER-2/neu, Ki-67, demonstrated a positive expression rate of >50%, which may help us to the diagnosis for SDC and revealing that SDC carcinogenesis may resemble that of breast ductal carcinoma or prostate cancer. As HER-2/neu blockers (trastuzumab) are shown to be effective in treatment of HER-2-overexpressing breast cancer, the same may be useful for the treatment of SDC. This therapeutic agent have shown positive results in a small number of cases of head and neck SDC (9,16).however, this requires additional research prior to the application of such therapies.

KEYWORDS

salivary duct carcinoma, salivary gland, Her2neu, prognostic factors.

INTRODUCTION:

Salivary duct carcinoma (SDC) is a distinct and rare primary malignancy of the salivary glands which accounts for <10% of all salivary malignancies Histolopathogically, it has resemblance to that of mammary duct carcinoma .(1-3).Though it was previously thought to be very rare, this entity is now considered to be less infrequent accounting for up to 2 % of all primary salivary neoplasms.

Patients are mostly above 50 years old with a male preponderance Male:Female ratio is 4:1(4). It mainly occurs in the parotid glands(17), although cases have been seen in the submandibular gland and very occasionally in the minor salivary glands (5).Being a very aggressive tumour the standard treatment regime for SDC is surgery in combination with radiotherapy, although the prognosis is not very well(6). The aim of our present retrospective study was to bring to light the clinicopathological characteristics of SDC as effective therapeutic protocol depends on a sufficient understanding of clinicopathological characteristics of SDC and its prognostic factors.

MATERIALS AND METHODS:

Between 2017 and 2021, in our tertiary care hospital out of 142 cases of salivary gland neoplasms, 11 cases of salivary gland neoplasms histopathologically diagnosed with SDC, were identified.

Cases of Salivary duct Carcinoma diagnosed on Histopathological Examination of ressected cases were taken. Cases of Salivary duct Carcinoma with insufficient Data or insufficient tissue were excluded. Haematoxilyn and eosin stained slides were examined and Immunohistochemistry was performed.

The Formalin-fixed, paraffin-embedded tissues were sectioned at 4 [mu]m. Sections were incubated overnight at room temperature. Deparaffinization and rehydration were performed using xylene and alcohol. The slides were submitted to microwave antigen retrieval for pretreatment (10 mM citrate buffer; pH, 6.0). Rinsing was done with 3 to 5 changes of distilled water followed by cooling at room temperature for 20 minutes Endogenous peroxidase was blocked with 3% aqueous hydrogen peroxide (ref-MAD021540Q-125)It was incubated with primary antibody for 30 minutes.

Statiscal Analysis:

All clinical and experimental data were statistically analyzed.

RESULTS:

All 11 patients primarily underwent surgical total parotidectomy followed by neck dissection followed by post-operative radiation therapy. All cases were followed up from the date of the surgical procedure to the date of mortality or the date patients were lost to follow-up.

11 cases of SDC in the head and neck during a 5 year period in a busy institution points that this cancer is rare. In the current cohort, the male:female gender ratio was 7:4 and the mean age of the patients was 65.8 years.

The parotid gland was the affected location in all our cases(eleven cases; 100%), Most (6) patients presented with mass larger than 5 cms and 7 patients had developed nerve paralysis. Six patients (54.5%) showed regional lymph node metastasis during routine neck dissection.

Grossly, the ressected masses were usually firm in consistency and ill defined with infiltration into the salivary gland and soft tissue with most cases presenting with lymph nodal extension.

Clinical and histological data were shown(Table I). In all our cases we had seen the presence of pleomorphic cells that form structures resembling distended ducts and solid nests. The frequently eosinophilic cells, often with apocrine differentiation, show nuclear pleomorphism, hyperchromasia and frequent mitoses.

Sections mostly showed combinations of solid, cribriform, papillary and comedo patterns, embedded in a desmoplastic, often hyaline, stroma. Cribriform growth patterns and in situ formations similar to those seen in ductal breast carcinoma were seen with papillary and cribriform intraductal component with comedonecrosis were also noted.

The invasive component consists of irregular glands and cords of cells that characteristically showed areas of desmoplastic reaction, which is similiar to that seen in invasive mammary ductal carcinoma.There were in situ component of cribriform pattern with comedonecrosis with presence of marked stromal desmoplasia. Lymphovascular and perineural invasion were seen in 63.6% and 63.6% of patients.(Fig 1).

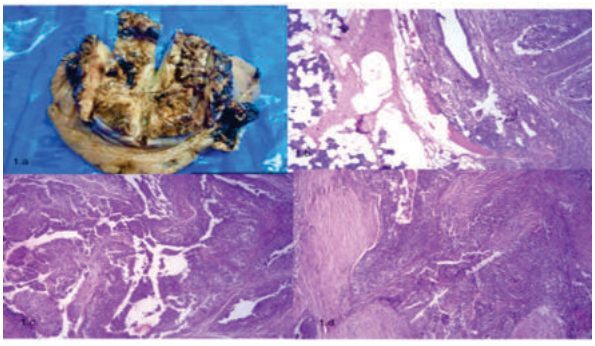

Figure 1.a: Gross photograph of Salivary duct Carcinoma.1.b: Scanner view showing normal parotid acini on left side and tumour areas on right side 1.c:Low power view showing glands lined by hyperchromatic pleomorphic cells 1.d: Low power view comedonecrosis can be appreciated and stromal desmoplastic reaction seen.

The results of the immunohistochemical analysis of the 11 samples are indicated in Table I. Examination of HER-2/neu protein expression revealed a high positivity rate of 81.8% (9/11 cases) in the examined tumor samples. However, Ki-67 showed >50% positive expression in 10 cases (Fig 2 & 3).

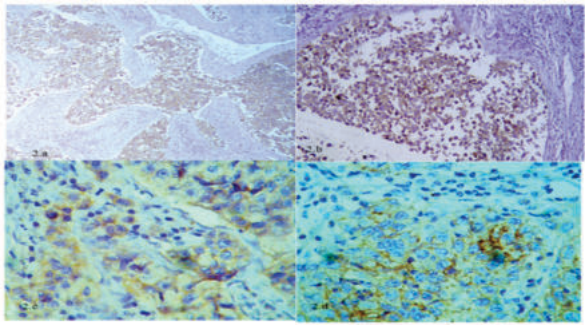

Figure 2.a: Her2neu expression at scanner view 2.b: At low power expression of Her2neu 2.c: Membranous positivity of Her2neu at 40x 2.d: Membranous positivity of Her2neu at 40x

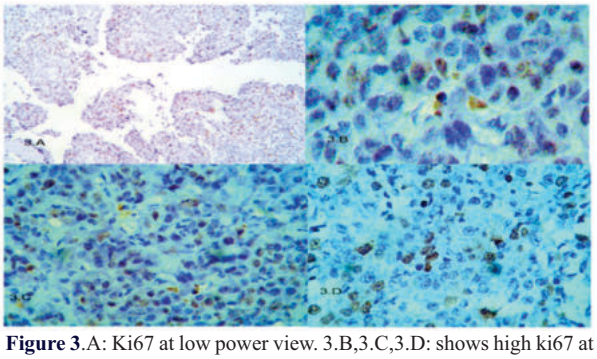

Figure 3.A: Ki67 at low power view. 3.B,3.C,3.D: shows high ki67 at higher power views.In our study, the range for the follow-up period was 10-45 months and 4 of the11 cases had succumbed to the disease, while distant metastasis noted in 3 patients, with the lung as the most common metastatic site.

Table 1. Clinical details

Clinical Details	Number of Cases	Percentage
Age, years : 35-60	6	54.5
Age, years : ≥61	5	45.4
Gender : Male	7	63.6
Gender : Female	4	36.3
Smoking Habit	7	63.6
Site : Parotid gland	11	100
Submandibular gland Palate	0	0
Nerve paralysis	7	63.6
Mortality due to disease	4	36.3

Table 2 : Operative details

Operative details	Number of Cases	Percentage
Total parotidectomy	11	100
Neck dissection	10	90.9
Post-operative radiation	9	81.9

Table 3 : Histological pattern

Histological pattern	Number of Cases	Percentage
Cribriform gland formation	11	100
Papillary structures	11	100
Comedonecrosis	11	100
Stromal desmoplasia	10	90.9
Lymphatic spread	7	63.6
Perineural spread	7	63.6
Intravascular tumor emboli	7	63.6
Surgical ressection margin Negative	10	90.9
Surgical ressection margin Positive	1	9.1

Table 4: TNM STAGING

T stage	Number of Cases	Percentage
T Stage 1	2	18.1
T Stage 2	3	27.2
T Stage 3	6	54.5
T Stage 4	0	0
N stage: N0	3	27.2
N stage ≥ N1	6	54.5
N stage: N2	2	18.1
Metastasis : M0	8	72.8
M1	3	27.2

Table 5: AJCC stage

HER-2/neu expression	Number of Cases	Batch no:
Positive	>3+ in 10 cases	
Negative:	1 case	

Table 6 : HER-2/neu expression

Ki67%	POSITIVE	NEGATIVE
>50%	3	-
25-50%	3	-
<25%	2	

Table 7 : Ki67%

AJCC stage	Number of Cases	Percentage
I :	2	18.1
II	1	9.0
III	6	54.5
IV	2	18.1

DISCUSSION:

SDC in the salivary gland region is a rare tumour which is histologically indistinguishable from mammary duct carcinoma, and showing intraductal and invasive components (2,3). Being a rare and an aggressive tumour limited experience is present to aid in guiding the development of novel treatment strategies for this cancer. SDC has been reported to occur with a male predominance with an average age of onset of ≥50 years (2,7).Our study also coroborrated with the findings of older age of onset(>60 years) and with male predominance.In our study all(100%) cases were seen in parotid gland and most of the patients (54.5%) of our patients presented with large mass which measured around 5 cm and it was firm to hard in consistency .7 out of 11 study subjects had nerve paralysis which is 63.6% of the cases(Table:1,2).All the data shows the aggresiveness of this tumour and are in keeping with previous studies.(2,3,6,17).Of the previous reported studies of patients with salivary duct carcinoma 5 year mortality is 55-65%(17,18).

Most of our cases (90.9%) at our institution are treated with Total parotidectomy with neck node dissection and the patients were also offered post operative radiotherapy. This study evaluated the major prognostic markers for SDC and found the relation of age, gender, size of tumour, nerve paralysis, post-operative radiation, T stage, N stage, AJCC stage, neck dissection in the 11 cases and this study also showed the expression of HER-2/neu, and Ki-67 in the salivary duct carcinoma so that the role of these can be added in treatment(Table:3,4,5,6 &7). SDC in parotid gland offered improved prognosis as compared to submandibular gland SDC(2,5) but this fact could not be coroborrated in the present study as all (100%) of our

cases were in the parotid gland .In the current series of patients, distant metastasis occurred in 3 patients, with the lung found as the metastatic site. Distant metastasis being one of major clinical problems in the management of SDC and requires the development of a novel alternative strategy to the current treatment methods.

Many previous studies have shown that HER-2/neu and p53 expression are statistically associated with SDC survival rates (3,9-14). High HER2 Neu expression is found in25-30% cases. (19)

In this study, the protein expression levels of HER-2/neu, Ki-67, demonstrated a positive expression rate of >50%, which may help us to the diagnosis for SDC.

Also the role of additional adjuvant therapy for SDC remains unclear till date. A systematic therapeutic method should be analysed in order to improve the prognosis of SDC as being a very aggresivetumour the limited efficacy and severe complications of surgery and radiotherapy prevails here. The present study demonstrated a high positivity rate for HER-2/neu and Ki67 expression in SDC, revealing that SDC carcinogenesis may resemble that of breast ductal carcinoma or prostate cancer (9,12,15,16). As HER-2/neu blockers (trastuzumab) are shown to be effective in treatment of HER-2-overexpressing breast cancer, the same may be useful for the treatment of SDC. This therapeutic agent have shown positive results in a small number of cases of head and neck SDC (9,16).however, this requires additional research prior to the application of such therapies.

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